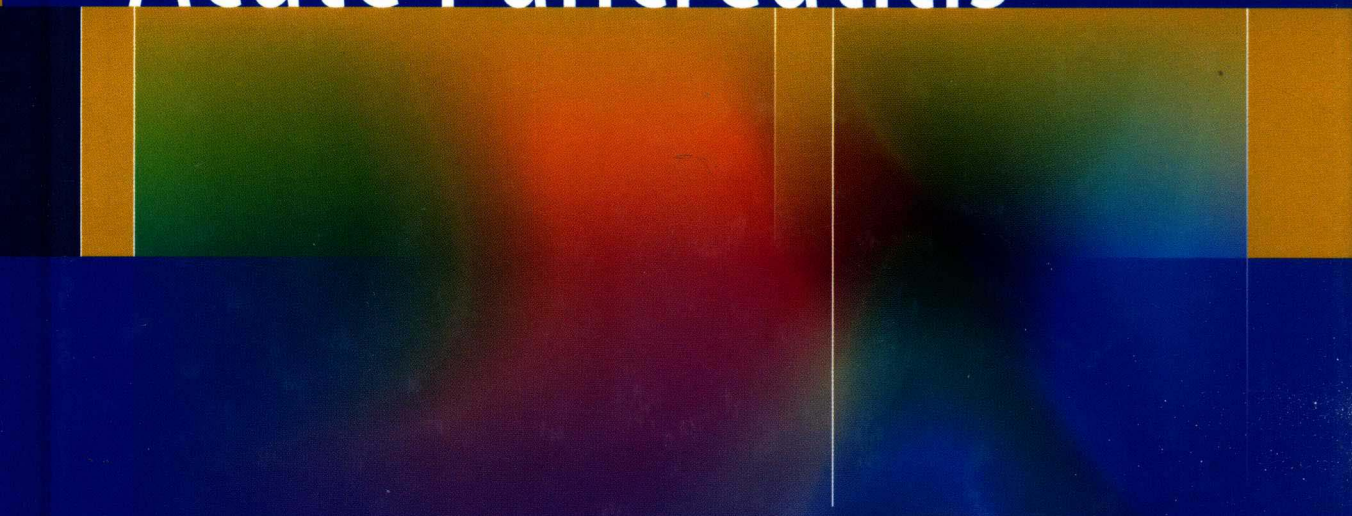
Prediction and Management of Severe Acute Pancreatitis



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Editors

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Preface

Severe acute pancreatitis (SAP) is a devastating disease affecting thousands of patients annually and resulting in substantial morbidity, mortality, and healthcare costs. In fact, acute pancreatitis is currently the most common hospital discharge diagnosis for gastrointestinal disease in the United States. While most patients have mild pancreatitis and recover, the high morbidity and a mortality rate of 20 % make SAP among the most lethal of all gastrointestinal diseases.

In the last 20 years extensive progress has been made in identifying and treating SAP. These advances include more standardized definitions of disease, more careful long-term follow-up of patient outcomes, and the beginnings of evidence-based therapies to prevent mortality and severe complications. Randomized, controlled trials are increasingly being performed to evaluate interventions in this disease, and consensus about definitions and therapies are being offered by major medical societies. Given the significant pathologic burden and improved diagnostic and therapeutic modalities, it is an important time for a text on severe acute pancreatitis.

This textbook provides a comprehensive review of the subject and serves as an essential resource for practicing gastroenterologists, surgeons, radiologists, intensivists, hospitalists, pathologists, and trainees. It details the recent consensus guidelines updating the definition of pancreatitis and its complications. It summarizes the current prediction models for severe acute pancreatitis, including laboratory, clinical, and imaging parameters. Evidence-based guidelines of medical and surgical management of both the hospitalized and discharged patient are described, with recommendations from expert authors pertaining to various clinical situations. Finally, complications of acute pancreatitis and their management, including the use of cutting-edge minimally invasive therapies, are discussed.

We offer our deep gratitude to our colleagues who authored chapters for this text. Their devotion to the field of pancreatology and their determination to improve the outcomes of patients afflicted with acute pancreatitis are inspiring. In editing this work, we were consistently reminded of how fortunate we are to collaborate with such dedicated clinicians and researchers.

We would also like to thank our editors at Springer, specifically Diane Lamsback, whose patience and guidance were critical in completing this book.

We hope you find the following text enriching and rewarding as we continue to make progress in the management and treatment of this difficult disease.

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Contents

Part I

Definitions of Severe and Necrotizing Pancreatitis

Revised Atlanta Classification of Acute Pancreatitis

1

Rupjyoti Talukdar and Santhi Swaroop Vege

Introduction

The introduction of the 1992 Atlanta Classification was a major milestone in the practice of pancreatology at that time [1]. The classification was aimed to define a common terminology and define the severity of the disease in a globally acceptable uniform manner. Even though it generated great enthusiasm initially, it was observed over the years that many issues pertaining to the disease were either not addressed or lacked clarity [2]. It was observed that over the past two decades, the terminologies from the Atlanta Classification were inappropriately used. For example, terms like pancreatic phlegmon and infected pseudocyst were still used, even after being abandoned in the Atlanta Classification. With generation of more data on the natural history and pathophysiology of the disease, and with development in cross-sectional imaging techniques, new terminologies like organized pancreatic necrosis, subacute pancreatic necrosis, necroma, and pseudocyst associated with necrosis came into existence [3]. These ambiguities called for a revision of the 1992 Atlanta Classification, which was long awaited in the pancreatology community. The process of revision was initiated in 2007 and after 5 long years of efforts that included modifications, revisions, and acquiring global consensus, the Revised Atlanta Classification was finally published in 2013 [4]. Table 1.1 shows the gross differences between the original and revised classification.

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Objectives of Revision

The objectives of the revision of the Atlanta Classification were to (1) incorporate modern concepts of the disease; (2) address areas of confusion; (3) improve clinical assessment of severity; (4) enable standardized data reporting; (5) assist objective evaluation of new treatments; and (6) facilitate communication among treating physicians and different institutions.

However, the revision was not meant to be a management guideline, even though the definitions have potential to guide appropriate management strategies.

Methodology

The Revised Atlanta Classification resulted from an international, web-based, multiply reiterative process that began in 2007 at the Digestive Diseases Week. The process began

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Table 1.1 Changes made in the Revised Atlanta validation compared to the 1992 Atlanta Classification

1992 Atlanta Classification	Revised Atlanta Classification
• No defined threshold of amylase/lipase levels for the diagnosis of AP	• Elevation of serum amylase and lipase of greater than three times the upper limit of normal is required to make a diagnosis
• Inclusion of local complications and/or organ failure under the severe category	• The presence of local complications in the absence of persistent organ failure is categorized as moderately severe acute pancreatitis
• No distinction between transient and persistent organ failure	• Transient organ failure is defined as organ failure that resolves within 48 h • Persistent organ failure is defined as organ failure that persists beyond 48 h
• Nonuniform use in the classification for organ failure	• Organ failure should be defined according to the Modified Marshall scoring system • Gastrointestinal bleeding as an organ failure has been removed
	• Discrete definitions of local complications (acute peripancreatic fluid collections, pancreatic pseudocyst, acute necrotic collection, and walled-off necrosis)
• No distinction of peripancreatic collections with and without necrotic debris	• Terms like pancreatic abscess have been abandoned
• Local complications included necrosis, abscess, and pseudocyst	• Terms like "organized pancreatic necrosis," "subacute pancreatic necrosis," "necroma," and "pseudocyst associated with necrosis," pancreatic sequestration are now collectively termed as walled-off necrosis

with a meeting of 40 selected pancreatologists and pancreatic surgeons to agree on the process and areas of revision. A working group, consisting of three pancreatic surgeons, two pancreatologists, and one pancreatic radiologist, prepared an initial draft. This was the first working document that was circulated among the 40 participants; the document was revised according to their suggestions. This working draft was then sent electronically to all members of 11 national and international organizations interested in acute pancreatitis. The working group prepared a second working draft after discussing the modification suggested in the first draft and resent to the members. The process was repeated and a third draft was generated, which contained minor modifications and was submitted to Gut. Based on journal reviewers' comments, a fourth revision of the document was made in which the three-tier classification of severity was incorporated.

Definition of a Diagnosis of Acute Pancreatitis

According to the Revised Atlanta Classification, a diagnosis of acute pancreatitis (AP) can be made if two of the following three features are present, namely abdominal pain consistent with AP (acute onset of a persistent, severe, epigastric pain often radiating to the back); serum lipase activity (or amylase activity) at least three times greater than the upper limit of normal; and characteristic findings of AP on contrast-enhanced computed tomography (CECT), magnetic resonance imaging (MRI), or transabdominal ultrasonography. Acute pancreatitis runs a dynamic clinical course and levels of serum lipase and amylase tend to fall over time. Therefore, in patients presenting after a prolonged duration following onset of symptoms, serum lipase and amylase may not be greater than three times the upper limit of normal in spite of typical pancreatitis type abdominal pain. These are the patients in which CECT could help in making the diagnosis. In situations where a diagnosis can be satisfactorily made on the basis of pain and serum lipase/amylase, CECT should be reserved for potential future use when it can diagnose local complications and provide important leads for complication-specific management approaches.

Phases of Acute Pancreatitis

The natural course of AP runs through two overlapping but pathophysiologically discrete phases. The early phase, which usually runs for 1–2 weeks, is clinically marked by systemic inflammatory response syndrome (SIRS) that is triggered by the cytokine cascade released as result of local pancreatic inflammation [5–7]. Persistent and severe SIRS during this phase could lead to development of transient or persistent organ failure [8, 9]. Persistent organ failure, which is defined as organ failure lasting for greater than 48 h primarily determines the severity of AP in the first phase [6, 9, 10]. Acute pancreatitis is a dynamic disease and local complications do develop during this phase; however, they are not proportional to the extent of organ dysfunction, thereby negating them as the predominant determinant of severity during this phase [11, 12]. Therefore, imaging with CECT or MRCP is unlikely to be of benefit in assessment and prognostication in this phase.

In the second or late phase, which can run a protracted course of weeks to months, the additional determinant of severity besides persistent systemic inflammation is local complications. This phase is also marked by a compensatory anti-inflammatory response syndrome (CARS), which makes the patient prone to infections that in turn can further determine severity by contributing to organ dysfunction. Therefore, besides clinical monitoring a meticulous evaluation of the local complications by appropriate imaging also becomes essential during this phase. Distinguishing between the different types of local complications would not only help to prognosticate but will also aid in selecting the appropriate treatment modality.

Types of Acute Pancreatitis

Acute pancreatitis can be divided into two broad categories, namely interstitial edematous pancreatitis (IEP) and necrotizing pancreatitis (NP); and this definition is predominantly directed by the degree of enhancement of the pancreas on CECT imaging (Table 1.2).

Interstitial Edematous Pancreatitis

In IEP, which constitutes 80–90 % of AP, CECT shows a relatively homogenously enhanced pancreas with or without mild peripancreatic stranding or peripancreatic fluid collection (Fig. 1.1a, b). However, it is important to understand that confirmation of IEP is not an indication for CECT.

Necrotizing Pancreatitis

Necrotizing pancreatitis, on the other hand, is characterized by tissue necrosis within the pancreatic parenchyma and/or peripancreatic tissues (Fig. 1.2a–c). Necrosis is marked by lack of enhancement, which is a function of impaired or absent tissue perfusion. Involvement of the pancreatic parenchyma alone is exceedingly uncommon and in most of the cases both the pancreatic parenchyma and peripancreatic tissues are involved. Peripancreatic necrosis alone (which is as frequent as pancreatic necrosis) results in a less severe disease course compared to involvement of the pancreatic parenchyma, but higher morbidity compared to IEP. Pancreatic and peripancreatic necrosis usually evolves over the first week of the disease and might not be mature enough to be detected early on by imaging. This is more so for peripancreatic necrosis, which is essentially necrosis of peripancreatic fat, which has little radiologically detectable perfusion even in health [13–16]. After 1 week, the necrosis will gradually liquefy and contain both solid and liquid components, thereby resulting in a more heterogeneous appearance that would make radiological diagnosis evident. Therefore, a diagnosis of NP can be most reliably made after about 1 week of development of AP.

Infected Necrosis

Infection of necrotic pancreatic and/or peripancreatic tissues usually occurs after the first week of AP. Most of the current evidence failed to establish a positive correlation between the extent of necrosis and the duration of symptoms with development of infected necrosis [11, 17–19].

Table 1.2 Definitions and CECT appearance

Terminology	Definitions	CECT appearance
Interstitial edematous pancreatitis (IEP)	• Acute inflammation of the pancreatic parenchyma and peripancreatic tissues, but without recognizable tissue necrosis	• Pancreatic parenchyma enhancement by intravenous contrast agent • No findings of peripancreatic necrosis
Necrotizing pancreatitis	• Inflammation associated with pancreatic parenchymal necrosis and/or peripancreatic necrosis	• Lack of pancreatic parenchymal enhancement by intravenous contrast agent and/or • The presence of findings of peripancreatic necrosis
APFC (acute peripancreatic fluid collection)	• Peripancreatic fluid associated with IEP with no associated peripancreatic necrosis. This term applies only to areas of peripancreatic fluid seen within the first 4 weeks after onset of IEP and without the features of a pseudocyst	• Occurs in the setting of IEP • Homogeneous collection with fluid density • Confined by normal peripancreatic fascial planes • No definable wall encapsulating the collection • Adjacent to pancreas (no intrapancreatic extension)
Pancreatic pseudocyst	• An encapsulated collection of fluid with a well-defined inflammatory wall usually outside the pancreas with minimal or no necrosis. This entity usually occurs more than 4 weeks after onset of IEP to mature	• Well circumscribed, usually round or oval homogeneous fluid density • No nonliquid component • Well-defined wall; that is, completely encapsulated • Maturation usually requires >4 weeks after onset of acute pancreatitis; occurs after IEP
ANC (acute necrotic collection)	• A collection containing variable amounts of both fluid and necrosis associated with necrotizing pancreatitis; the necrosis can involve the pancreatic parenchyma and/or the peripancreatic tissues	• Occurs only in the setting of acute necrotizing pancreatitis • Heterogeneous and nonliquid density of varying degrees in different locations (some appear homogeneous early in their course). • No definable wall encapsulating the collection • Location—intrapancreatic and/or extrapancreatic
WON (walled-off necrosis)	• A mature, encapsulated collection of pancreatic, and/or peripancreatic necrosis that has developed a well-defined inflammatory wall. WON usually occurs >4 weeks after onset of necrotizing pancreatitis	• Heterogeneous with liquid and nonliquid density with varying degrees of loculations (some may appear homogeneous) • Well-defined wall, that is, completely encapsulated • Location—intrapancreatic and/or extrapancreatic • Maturation usually requires 4 weeks after onset of acute necrotizing pancreatitis

Since development of infected necrosis has several therapeutic implications, it is essential to recognize it early [18]. The telltale sign of infected necrosis is the presence of extraluminal gas in pancreatic or peripancreatic tissues on CECT (Fig. 1.3a, b), although gas can be present without infection due to a communication with the gut. In such communications, one could presume infection still exists